Studies of Reactions of Amines with Sulfur Trioxide. V.[1] Transsulfonation of Amine Salts of Some *N*-Substituted Amidosulfuric Acids

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4-Methylanilinium butylamidosulfate, butylammonium (4-methylphenyl)amidosulfate, and 4-methylanilinium (4-methylphenyl)amidosulfate were heated separately under reduced pressure at different temperatures ranging from 80 to 180 °C. Butylammonium butylamidosulfate was heated with 4-methylaniline under atmospheric and reduced pressure. The product compositions were determined as functions of reaction time and temperature, and the components were separated and identified. At lower temperatures (4-methylphenyl)amidosulfate and 4-methylaniline-*N*,2-disulfonate were the major products, while at higher temperatures 4-methylaniline-2-sulfonate and 2,6-disulfonate were the major products. The ease of N–S bond cleavage of the amidosulfate salts ($RNHSO_3^-R'NH_3^+$) (**1**) depends largely on the basicity of both the parent amine (RNH_2) (**2**) and the salt-forming base ($R'NH_2$) (**3**). The results suggest that the initial step of the transsulfonation involves the dissociation of **1** into **3** and the free acid followed by an equilibration between $RNHSO_3H$ and $RNH_2^+SO_3^-$ (**4**). It is considered that **4** may be the sulfonating species and the free amines, **2** and **3**, should be the receptors of a sulfonate group. In contrast to the widely accepted scheme (transsulfonation and subsequent intramolecular rearrangement), our results show that both the transsulfonation and the rearrangement process occur concurrently and the same type of mechanism (a bimolecular displacement, *viz.*, $B^+: SO_3^- + B': \rightleftarrows B^+: + B^+: SO_3^-$) may be operative.

Paal and his co-workers first studied the reaction of amidosulfuric acid with a variety of amines.[2a-d] This reaction was later reinvestigated in detail by Quilico.[3] He found that amidosulfuric acid reacts at a water-bath temperature with an aromatic amine such as aniline, 4-methylaniline, or 1-naphthylamine, producing the corresponding ammonium arylamidosulfate, which in turn rearranges to the ring sulfonate at higher temperature (>150 °C). Recently, it has also been reported that the reaction of butyl- and cyclohexylamidosulfuric acids and their salts with a large excess of aniline, *N*,*N*-dimethylaniline, or anisole gave the corresponding *p*-sulfonic acids in high yields.[4] On the other hand, Saito, Dehara, and Manabe[5] demonstrated that the reaction between amidosulfuric acid and aniline gave a mixture of aniline-2- and 4-sulfonic acids along with a small amount of aniline-2,4- and 2,6-disulfonic acids whose composition depended on the reaction conditions.

Although it is well documented that arylamidosulfates rearrange to the corresponding ring sulfonates,[6,7] the mechanism of the rearrangement has been unsettled.[8-10] Furthermore, the intermediacy of phenylamidosulfuric acid in the sulfonation of aniline with concentrated sulfuric acid or by "baking" has been discussed for many years by many workers,[8-10] but so far phenylamidosulfuric acid has neither been isolated from such reactions nor been synthesized as such.[11]

We, therefore, undertook the thermal reaction of butylammonium and 4-methylanilinium salts of both butylamidosulfuric acid and (4-methylphenyl)amidosulfuric acid in order to gain an insight into the nature of the transsulfonation of *N*-substituted amidosulfates.

Results and Discussion

Isolation and Identification of the Reaction Products. 4-Methylanilinium butylamidosulfate (**5**), butylammonium (4-methylphenyl)amidosulfate (**9**), and 4-methylanilinium (4-methylphenyl)amidosulfate (**11**) were heated separately under reduced pressure at temperatures ranging from 80 to 180 °C. Butylammonium butylamidosulfate (**1**) was, in addition, heated with 4-methylaniline. The product composition depended on both the reaction time and temperature. Namely, (4-methylphenyl)amidosulfate (**9**) and 4-methylaniline-*N*,2-disulfonate (**13**)[12] were the major products at lower reaction temperatures, whereas 4-methylaniline-2-sulfonate (**12**) and 4-methylaniline-2,6-disulfonate (**15**) were the major products at higher temperatures. In no run was any chromatographic evidence obtained for the formation of 4-methylaniline-3-sulfonic acid and the 2,5-disulfonic acid. Each component was separated (as the sodium salts) by preparative liquid chromatography (cellulose Whatman CF-11, dioxane–H_2O 4: 1 and 5: 1 v/v as the developing solvent). **9** and **13** were then converted to the corresponding tetraphenylphosphonium salts and identified by elemental analysis, melting points (mixed mp), and comparison of their IR spectra with those of authentic samples. **12** and **15** were converted to the corresponding hexylammonium salts and identified similarly.

Product Analysis. Quantitative analysis of the reaction products was achieved by the combination of ion-exchange chromatography and chemical analysis (see the Experimental section). Use of quarternary ammonium-type resin-Amberlite CG 400 (Cl^- form) gave unsatisfactory results because this resin had excessively large distribution coefficients.

Thin-layer chromatography (TLC) was used in each run for qualitative analysis. The best resolution was obtained on cellulose with a dioxane–water (3: 1—4: 1 v/v) solvent system. The R_f values for isomeric 4-methylanilinemonosulfonic and disulfonic acids (spotted as their sodium salts) are listed in the Table.

Tetraphenylphosphonium Salts. The tetraphenylphosphonium salts of (4-methylphenyl)amidosulfuric

TABLE. R_f VALUES AND SPECTRAL DATA OF 4-METHYLANILINESULFONIC ACIDS

Compound	R_f[a)]	Color of spot	IR spectra (cm^{-1})
4-$MeC_6H_4NHSO_3Na$	0.63	orange	3260, 1512, 1198, 1061, 910, 810
2-SO_3Na-4-$MeC_6H_3NH_2$	0.54	reddish orange	3400, 3320, 1625, 1503, 1223, 1184, 1109, 1036, 817, 735, 701
3-SO_3Na-4-$MeC_6H_3NH_2$	0.42	red	1617, 1491, 1207, 1195, 1090, 1030, 886, 812, 717
2-SO_3Na-4-$MeC_6H_3NHSO_3Na$	0.34	reddish orange	1493, 1388, 1202, 1094, 1067, 1056, 1028, 914, 875, 832, 706
2,6-$(SO_3Na)_2$-4-$MeC_6H_2NH_2$	0.19	yellow	1630, 1475, 1182, 1123, 1039, 883, 807, 744
2,5-$(SO_3Na)_2$-4-$MeC_6H_2NH_2$	0.09	dark red	1481, 1395, 1203, 1132, 1033, 894, 655

a) 0.25 mm-thick cellulose plate; dioxane–water (15: 4 v/v). For details see the Experimental section.

acid and 4-methylaniline-*N*,2-disulfonic acid were soluble in non-polar solvents such as chloroform and carbon tetrachloride as well as in polar solvents. This solubility behavior is in marked contrast with that of the corresponding alkylammonium and metal salts. Furthermore, it is noteworthy that the phosphonium salts were remarkably stable toward hydrolysis, being comparable to the metal salts; that is, no hydrolysis was observed even after 0.5 h boiling of each saturated aqueous solution. This is in accord with the view that the amidosulfate ion ($R^1R^2NSO_3^-$) is indeed the unreactive species in the hydrolysis of the salts of amidosulfuric acid and its *N*-substituted derivatives, while the zwitterion ($R^1R^2NH^+SO_3^-$) is most probably the reactive species.[9)]

*Reaction of Butylammonium Butylamidosulfate (**1**) with 4-Methylaniline (**6**).* When **1** was heated with **6** for 8 h under atmospheric pressure at different temperatures ranging from 120 to 180 °C, transsulfonation proceeded remarkably slowly. Thus, even after 8 h at 180 °C transsulfonation occurred only to the extent of 50%, to give (4-methylphenyl)amidosulfate (**9**) (40%) and 4-methylaniline-2-sulfonate (**12**) (6%) (Fig. 1). In marked contrast, the reaction was fast under reduced pressure. After 8 h at 150 °C **9** reached its maximum (80%) yield. At higher temperatures 4-methylaniline-2,6-disulfonate (**15**) as well as **12** were also formed at the expense of **9** (Fig. 1).

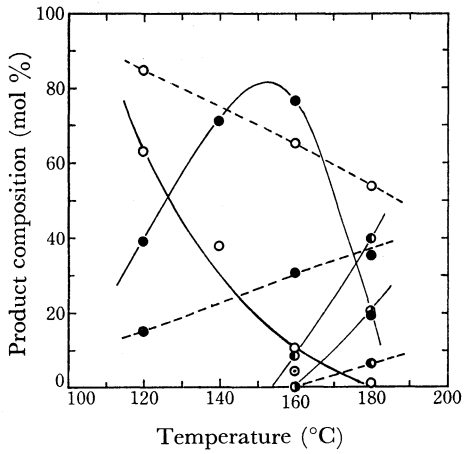


Fig. 1. Reaction of butylammonium butylamidosulfate with 4-methylaniline under atmospheric (-----) and reduced (——) pressure.
Molar ratio 1: 1.1—1: 1.3, reaction time 8.5 h.
○: $BuNHSO_3^-$, ●: $MeC_6H_4NHSO_3^-$, ◐: $MeC_6H_3(SO_3^-)NH_2$, ⊙: $MeC_6H_3(SO_3^-)NHSO_3^-$, ◑: $MeC_6H_2(SO_3^-)_2NH_2$. The same symbols are used in all figures.

In order to gain a better understanding of the reaction path, the variation of product distribution with reaction time was followed (Fig. 2). In the first stage **1** was consumed rapidly and **9** was correspondingly formed. Two hours after the start of the reaction, the maximum (68%) yield of **9** was obtained. Beyond this point, **9** also decreased monotonically and **12** was formed instead. After 8.5 h **1** disappeared almost completely. **12** and **15** were the major products.

It is worthwhile noting the formation of 4-methylaniline-*N*,2-disulfonate (**13**), because the intermediacy of aniline-*N*,2- and *N*,4-disulfonic acids in the sulfonation of aniline with concentrated or fuming sulfuric acid has recently been discussed.[10)] Although the formation of such compounds has already been reported,[7)] no isolation was achieved. We isolated **13** successfully by preparative liquid chromatography.

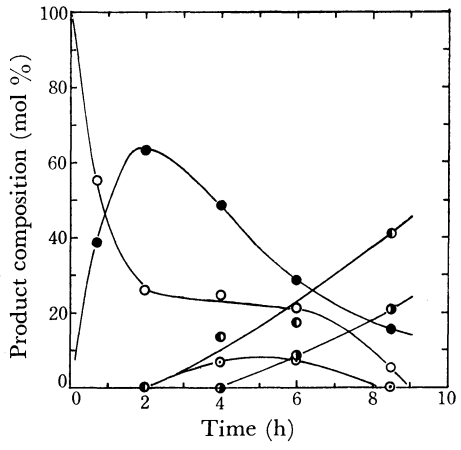


Fig. 2. Variation of product composition with reaction time in the reaction of butylammonium butylamidosulfate with 4-methylaniline at 180 °C under reduced pressure. Molar ratio 1: 1.1—1: 1.3.

*Reaction of 4-Methylanilinium Butylamidosulfate (**5**).* If the initial step both in the transsulfonation[13)] and in the rearrangement[13)] involves the dissociation into the free amidosulfuric acid (the reactive species) and the amine, it is to be expected that the rates of transsulfonation and rearrangement should increase with a decrease in the basicity of the salt-forming amine (to be discussed later).

As expected, transsulfonation of **5** was fast as compared with the reaction between **1** and **6**. Thus, the reaction

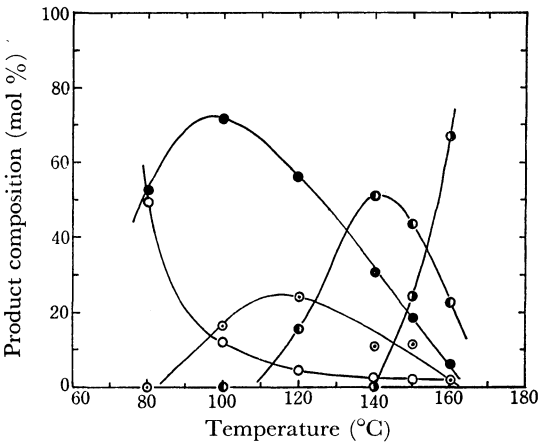


Fig. 3. Thermal reaction of 4-methylanilinium butylamidosulfate under reduced pressure. Reaction time 8.5 h.

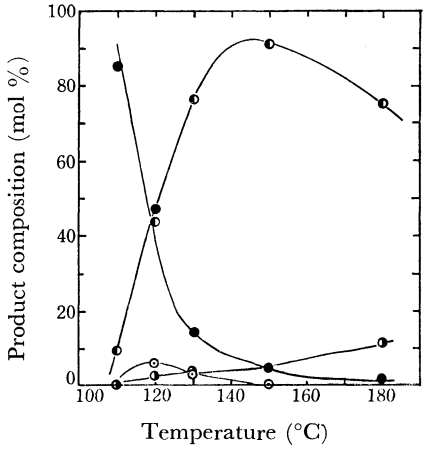


Fig. 5. Thermal reaction of 4-methylanilinium (4-methylphenyl)amidosulfate in *o*-dichlorobenzene. Reaction time 4 h. The reaction at 180 °C was conducted without solvent under reduced pressure.

of **5** at 80 °C for 8.5 h led to 52% conversion of **5** into **9**, and after 8.5 h at 120 °C **5** had disappeared almost completely (Fig. 3). It should be noted here that the reaction at 100 °C gave rise to the formation of **13** (17%), while no **12** was detected in the product mixture (TLC).

Thermal Rearrangement of Butylammonium (4-Methylphenyl)amidosulfate (9). **9** was heated for 8.5 h under reduced pressure in the temperature range 120—160 °C. The variation of product composition with reaction temperature is illustrated in Fig. 4. The rearrangement occurred only at temperatures above 120 °C, whereas with **5** the rearrangement to the ring sulfonate **13** took place far below 120 °C.

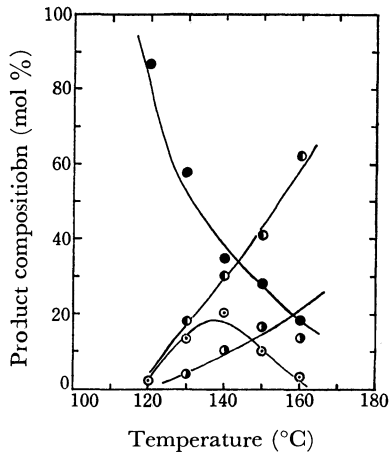


Fig. 4. Thermal reaction of butylammonium (4-methylphenyl)amidosulfate under reduced pressure. Reaction time 8.5 h.

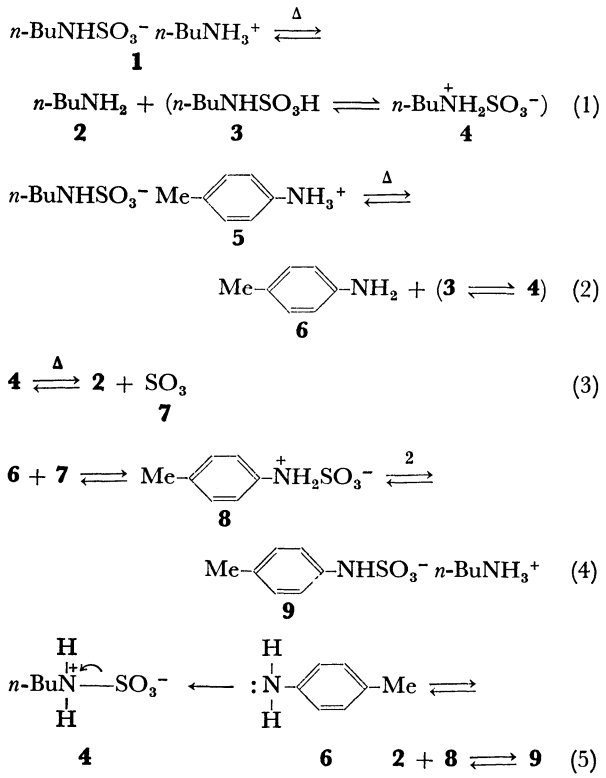
12 and **15** increased with an increase in temperature. The total yield of **12** plus **15** amounted to 80% at 160 °C. **13** was also formed up to 20%.

Thermal Rearrangement of 4-Methylanilinium (4-Methylphenyl)amidosulfate (11). The rearrangement of **11** was very rapid as compared with that of **9** (Fig. 5); after 4 h at 120 and 130 °C **11** rearranged to the extents of 45 and 85% respectively, yielding **12** (main product) along with **13** and **15**. A maximum yield of **12** was obtained from the reaction at 150 °C for 4 h. At 180 °C, a considerable amount (11%) of **15** was formed. Shortening of the reaction period to 35 min improved the yield of **12** (95%); only a trace of **15** was formed. This fact suggests that **15** can be formed not only by direct sulfonation of **12** with **8** (Eq. 16), but also by disproportionation of **12** (Eq. 17).[7]

Mechanistic Considerations. It is well known[14] that anhydrous metal salts of amidosulfuric acid and its *N*-substituted derivatives are much less reactive[4,14-16] than the corresponding ammonium salts[4] and the free acids[3-5,11,17] towards nucleophilic N–S bond cleavage (sulfonation, sulfamation, sulfation, hydrolysis, *etc*). Striking differences in reactivity of the N–S bond between the ammonium or amine salts and the metal salts can be explained in terms of the thermal dissociation of the former salts into the free amidosulfuric acid and the base. For the latter salts such type of dissociation is impossible. However, if a proton donor such as anilinium chloride, water, or a mineral acid is added in the reaction system,[7,15,18] then metal salts can also undergo the N–S bond cleavage. It has been proved that the salts of amidosulfuric acids exist as the true amidosulfate ions ($R^1R^2NSO_3^-M^+$),[19a,b] whereas the corresponding free acids exist as the zwitterions ($R^1R^2NH^+SO_3^-$).[19a,b,d]

All these results strongly suggest that an amidosulfate ion as such is more or less stable, although its stability is dependent on the nature of the *N*-substituent, whereas its *N*-protonated form (the zwitterion) is most probably the reactive species in acid-catalyzed hydrolysis,[9] solvolysis,[20] and transsulfonation.[4,18] Undoubtedly the heterolysis of the N–S bond of the zwitterion should be facilitated by the positive charge on the amido-nitrogen atom, because R^1R^2NH (neutral molecule) is a much better leaving group than $R^1R^2N^-$ (amide ion).

The initial step in both the transsulfonation and the rearrangement of the amine salts of the amidosulfuric



Scheme 1.

acids is presumably the dissociation of the salt into the amidosulfuric acid[21] and the salt-forming base (Eqs. 1, 2, 6, and 7). Support for this assertion was provided by the following observations: (1) in most of the runs carried out under reduced pressure, boiling of the reaction mixture and refluxing of **6** were observed immediately after the reaction had started; (2) under reduced pressure, transfer of the *N*-sulfonate group from **1** to **6** occurred much faster than it did under atmospheric pressure (Fig. 1); (3) the rates of transsulfonation and rearrangement increased with an increase in the acidity of the conjugate acid of the salt-forming base (compare Fig. 1 with Fig. 3, and Fig. 4 with Fig. 5).

Two possible types of mechanisms for the transsulfonation may be considered: (1) a dissociative mechanism (Eqs. 3 and 4) and (2) a bimolecular nucleophilic substitution (Eq. 5). It should be noted here that the transsulfonation with **5** occurred at such a low temperature that zwitterion **4** was quite stable. For example, at 100 °C for 8.5 h, **5** underwent transsulfonation to the extent of 80% to give **9** (72%) and **13** (16%).

Thermal decomposition of amidosulfuric acid[22] occurs only above its melting point (*i.e.*, at 210—220 °C). The most probable reaction has been considered to involve a chain condensation followed by cyclization to polysulfimide.[22] Cleavage of the N–S bond in this thermolysis probably takes place only through the hydrolysis with the water molecules released on the condensation and not through a pyrolytic process.

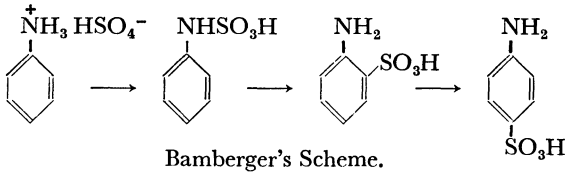
$$n\mathrm{NH_2SO_3H} \longrightarrow \mathrm{NH_2(SO_2NH)_{n-1}SO_3H} + (n-1)\mathrm{H_2O}$$
$$\longrightarrow (\mathrm{NHSO_2})_n + n\mathrm{H_2O}$$
$$\mathrm{NH_2SO_3H} + \mathrm{H_2O} \longrightarrow \mathrm{NH_4HSO_4}$$

The gas-phase reaction of sulfur trioxide with an amine such as trimethylamine is extremely exothermic.[23] Therefore, the N–S bond energy of $R^1R^2R^3N^+–SO_3^-$ must be very high. Accordingly the dissociative process seems to be unlikely.

On the other hand, it is well documented[20] that amidosulfuric acid and its *N*-substituted derivatives undergo cleavage of the N–S bond in a polar aprotic solvent such as pyridine, dioxane, DMF, *etc.* under mild conditions. It is, therefore, reasonable to assume that the transsulfonation proceeds through the latter process.

The rearrangement of phenylamidosulfuric acid to the ring sulfonic acid(s) has been performed by use of its salts under a variety of reaction conditions.[10] However, only a few papers have been published on the mechanism of thermal rearrangement of *neat* arylamidosulfates.[7]

Three possibilities may be considered for the mechanism of the rearrangement. The first possible mechanism is the intramolecular pathway postulated originally by Bamberger and Kunz[24] for the sulfonation of aniline. This scheme was later disproved experimentally.[25]



Bamberger's Scheme.

Furthermore, the formation of 2,6-dimethylaniline-4-sulfonate in the thermal rearrangement of 2,6-dimethylanilinium butylamidosulfate[26] cannot be explained by the intramolecular mechanism.

The second mechanism is an intermolecular process which involves thermal dissociation of **8** to **6** and **7**, followed by ring sulfonation of **6** with **7** (Eq. 8).

In view of the hydrolytic and thermal instability of **10**[11,14] thermal cleavage of the N–S bond may take place.

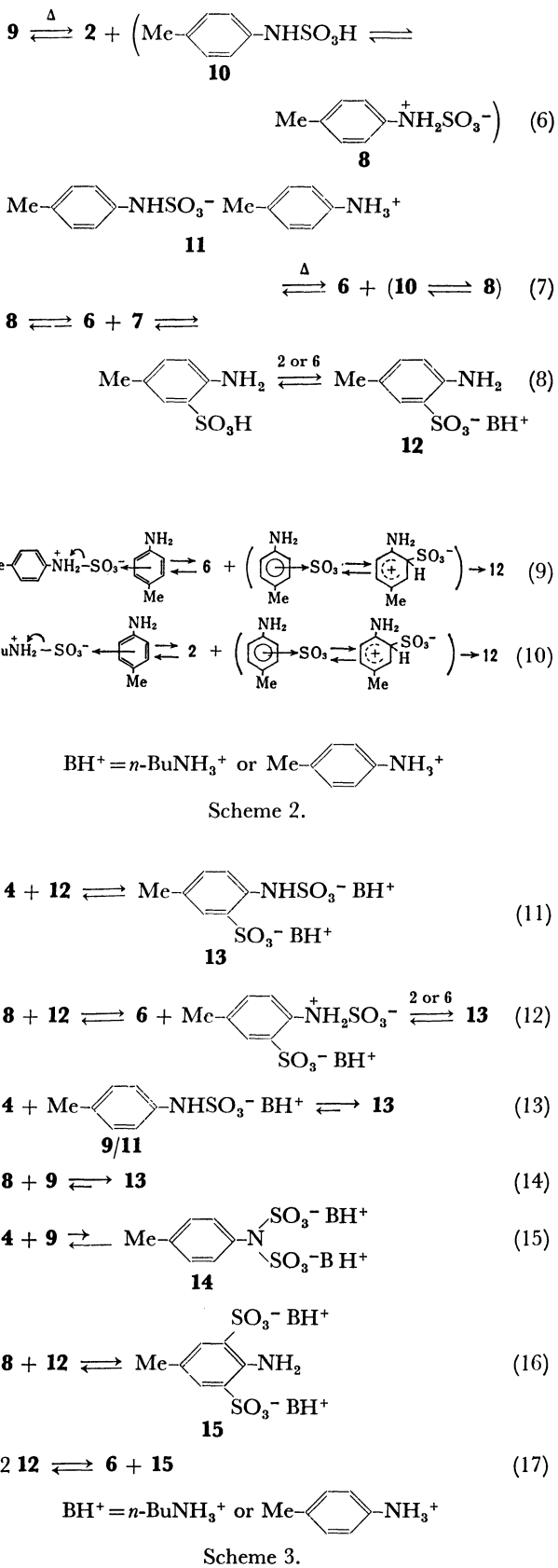
The third possible mechanism involves a bimolecular substitution at the sulfur atom (Eqs. 9 and 10). Since no traces of 4-methylaniline-3-sulfonate (*m*-sulfonation) could be detected (TLC) in the product mixture in any of our experiments, the free amine **6** and/or **10** but not the *N*-protonated species **8** must be the receptor of a rearranging *N*-sulfonate group.

Comparison of the data for the thermal rearrangment of **5** (Fig. 3) and **9** (Fig. 4) shows that conversion of **5** into **12** is much faster than that of **9** into **12**; thus, reaction of **5** at 120 °C for 8 h led to the formation of the rearrangement products **12** (16%) and **13** (24%), in addition to **9** (56%).[28] On the other hand reaction of **9** did not give **12** under the same conditions, and even after 8 h at 160 °C, 18% of **9** remained unchanged.

These results cannot be interpreted on the basis of the widely accepted sequence:[2c,3]

$$\mathrm{ArNH_2} + \mathrm{\overset{+}{N}H_3SO_3^-} \longrightarrow \mathrm{NH_2SO_3^-}\,\mathrm{ArNH_3^+} \longrightarrow$$
$$\mathrm{ArNHSO_3^-}\,\mathrm{NH_4^+} \longrightarrow o\text{- and/or } p\text{-Arenesulfonic acid}$$

A probable explanation involves concurrent pathways: The *N*-sulfonation of **6** with **4** to give **9** (Eq. 5) and the direct ring-sulfonation of **6** with **4** (Eq. 10) followed by sulfonate-group transfer from **4** and/or **8** to **12**

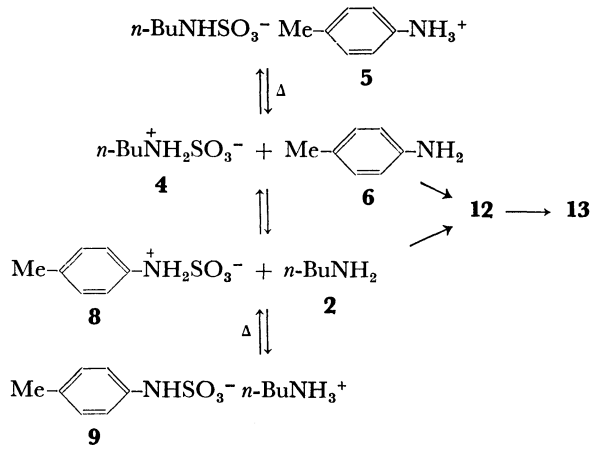


Scheme 2.

Scheme 3.

(Eqs. 11 and 12).

A dissociation equilibrium between the amidosulfate ion and the zwitterion should depend greatly on the acidity of the conjugate acid of the salt-forming amine; namely, this equilibrium shifts toward the zwitterionic form as the acidity of the conjugate acid of the amine increases[29] and thus the differences in reactivity between **5** and **9** can be accounted for by the following scheme:



On the other hand, the strength of the N–S bond of an *N*-substituted amidosulfuric acid is expected to increase as the basicity of the parent amine increases. The considerable differences in the rate of rearrangement between **5** and **11** (Figs. 3 and 4) can be explained in terms of the differences in reactivity between the reactive species **4** and **8**.

Several pathways for the formation of **13** may be considered. However, it seems most probable that **13** is formed by reaction(s) between **4** and **12**, and/or between **8** and **12** (Eqs. 11 and 12), since it has been well known that, in the presence of a proton donor such as anilinium chloride, the *N*-sulfonate group on an aromatic amine is transferred readily to another aromatic amino-nitrogen.[7,18]

Ring sulfonation of **9** (Eqs. 13 and 14) at as low as 100 °C seems less probable, since **9** should be much less reactive than **12**. This process may, however, operate at higher temperatures.[27]

(4-Methylphenyl)imidobis(sulfate) (**14**) could neither be isolated nor detected. This can be accounted for in terms of the great degree of steric strain due to the over-crowding around the imido-nitrogen atom.[30]

Experimental

All the melting points were measured in sealed capillaries and uncorrected. The dioxane was of chromatographic grade. The butylamine and 4-methylaniline were guaranteed reagents and used as received. The IR spectra were recorded for KBr discs on a JASCO IR-S spectrophotometer. DEAE-cellulose (Serva, hydrochloride form) was suspended in deionized water and allowed to stand for 20—40 min, and the supernatant was discarded; this process was repeated several times. The exchanger was then suspended in 3M NaCl, packed in a column, and washed with water. Thin-layer chromatography was performed on 0.25 mm-thick cellulose plates (cellulose mikrokristallin, E. Merck) by use of a dioxane–water (15:4 v/v) solvent system. Components were located by inspection under UV light or by placing the plate in a container filled with nitrous gases, followed by spraying with 1-naphthol-4-sulfonic acid and subsequent exposure to ammonia gas.

Reaction Runs. In a test tube (150×14 mm) equipped with a stopcock was placed a weighed amount of a substrate (2 mmol). The test tube was evacuated (*ca.* 20 Torr) with a water aspirator for a very short period (*ca.* 10 s) and the stopcock was closed. The test tube was then heated in a thermostated oil bath. After the reaction was complete, the product mixture was cooled and dissolved in a dilute sodium hydroxide solution. The solution was extracted three times with 2-ml portions of benzene to remove the unreacted 4-methylaniline. The aqueous solution was evaporated *in vacuo*. The residual solid was dissolved in deionized water and the solution was passed through a column (180×9 mm i.d.) of Dowex 50WX4 (Na^+ form). The eluate was collected into a volumetric flask and diluted accurately up to 100 ml. Aliquots of this stock solution were employed for the following product analyses.

Determination of Product Composition. The quantities of each component (**A**—**F**) were calculated from the determinations given below: *n*-$BuNHSO_3Na$ (**A**), 4-$MeC_6H_4NHSO_3Na$ (**B**), 2-SO_3Na-4-$MeC_6H_3NHSO_3Na$ (**C**), 2-SO_3Na-4-$MeC_6H_3NH_2$ (**D**), 2,6-$(SO_3Na)_2$-4-$MeC_6H_2NH_2$ (**E**), Na_2SO_4 (**F**).

Butylamidosulfate and (4-Methylphenyl)amidosulfate: An aliquot (5 or 10 ml) was pipetted on a column (164×13 mm i.d.) of DEAE-cellulose. The column was rinsed with 0.5 ml of distilled water and then eluted with 0.15 M NaCl at a flow rate of 0.25—0.3 ml/min. The first fraction containing **A** was eluted at 30—37 ml and the second fraction containing **B** at 42—48 ml. Each fraction was treated with 3 M HCl (1 ml) and 6 M $NaNO_2$ (0.2 ml). Sulfate ion thus formed was precipitated with 0.01 M $BaCl_2$ (10 or 20 ml) and the excess of barium ion was back-titrated with 0.01 M EDTA; (**A** and **B**).

Total Sulfonate-group Bound to Aromatic Amino-nitrogen: To an aliquot (5 or 10 ml) was added 0.01 M $BaCl_2$ (10 or 20 ml). The volume of the solution was adjusted to *ca.* 20 ml by dilution or evaporation. 3 M HCl (1 ml) was then added and the solution was boiled for 20 min and cooled.[31] The barium sulfate was filtered off and the excess of barium ions in the filtrate titrated; (**B**+**C**+**F**).

Total N-Sulfonate Group: To an aliquot (5 or 10 ml) were added successively 3 M HCl (1 ml), 0.01 M $BaCl_2$ (10 or 20 ml), and 6 M $NaNO_2$ (0.2 ml). After the solution had been left for 1 h, urea (*ca.* 0.1 g) was added. The solution was left again for 1 h, and then heated for 30 min; the precipitate was removed by filtration; the excess of barium ion was titrated; (**A**+**B**+**C**+**F**).

Sulfate Ion Formed in the Reaction: To an aliquot (10 ml) 0.01 M $BaCl_2$ (10 ml) and 3 M HCl (1 ml) were added at room temperature. The solution was filtered directly into an Erlenmeyer flask containing 0.1 M Zn-EDTA (10 ml) and ammonium chloride buffer solution (pH 10) (1 ml). The excess of barium ion was titrated with 0.01 M EDTA; (**F**).

4-Methylaniline-N,2-disulfonate plus 4-Methylaniline-2-sulfonate and 4-Methylaniline-2,6-disulfonate: The remainder of the stock solution after the above analyses was concentrated to *ca.* 20 ml. After addition of 3 M HCl (2 ml), the mixture was boiled for 20 min, cooled, and evaporated *in vacuo*. The residue was dissolved in hot water (20 ml). Barium hydroxide was then added in a slight excess in order to remove sulfate ions. After filtration, the filtrate was passed through a cation-exchange column (Amberlite IR 120 H^+-form) and the eluate was evaporated to dryness. Trituration of the residue with a minimum volume of ethanol gave 4-methylaniline-2-sulfonic acid (**C**+**D**); evaporation of the ethanol solution gave 4-methylaniline-2,6-disulfonic acid (**E**). The 2- and 2,6-acids were then titrated with 0.05 M NaOH.

Material. Butylamidosulfuric Acid: This compound was prepared by the action of butylamine on chlorosulfuric acid in 1,2-dichloroethane at −10—0 °C; mp 173.5—174.5 °C (decomposed with effervescence) (lit,[32] 177—178 °C). IR: 3125 (N–H, br, s), 1527 (NH_2^+, m), 1299 (NH_2^+–SO_3^-, s), 1246 (NH_2^+–SO_3^-, s), 1080 (SO_3^-, m), 1066 (SO_3^-, m), 835 (m), 770 (m), and 715 cm^{-1} (S–N, m). Found: N, 9.12; S, 21.04%. Calcd for $C_4H_{11}O_3NS$: N, 9.14; S, 20.93%.

Butylammonium Butylamidosulfate (1): This was prepared by neutralization of the free acid with butylamine in methanol. After recrystallization from ethyl methyl ketone, it melted at 125.5—127 °C (lit,[32] 127—128 °C). IR: 2950 (NH_2^+, m), 1465 (m), 1186 (SO_3^-, s), 1041 (SO_3^-, s), 910 (w), and 740 cm^{-1} (br, w). Found: N, 12.36; S, 14.13%. Calcd for $C_8H_{22}O_3N_2S$: N, 12.38; S, 14.16%.

4-Methylanilinium Butylamidosulfate (5): A slight excess of 4-methylaniline was added to a solution of butylamidosulfuric acid in methanol. The mixture was evaporated *in vacuo* and the residual solid was washed three times with benzene and dried in a desiccator. Colorless *crystals*; the melting point depended on the rate of heating. IR: 3260 (N–H, w), 2930 (NH_2^+, br, s), 1187 (SO_3^-, s), 1043 (SO_3^-, br, s), and 817 cm^{-1} (2H, m). Found: N, 10.68; S, 12.35%. Calcd for $C_{11}H_{20}N_2O_3S$: N, 10.76; S, 12.31%.

Barium (4-Methylphenyl)amidosulfate: 4-Methylanilinium amidosulfate (30 g), prepared by neutralization of amidosulfuric acid with 4-methylaniline in methanol, was heated with 4-methylaniline (45 g) at 100 °C for 3.5 h. After cooling, benzene (50 ml) was added. The solid was collected, washed with benzene, and recrystallized from water to give the pure *ammonium salt*. This was dissolved in hot water and treated with a slurry of barium hydroxide. The mixture was filtered and the residue was washed repeatedly with hot water. The filtrate and washings were combined and evaporated to dryness *in vacuo*. The residual solid was dissolved again in hot water (500 ml) and carbon dioxide was passed through the solution to remove the excess of barium hydroxide. The filtered solution was left overnight at room temperature. The *product* separated out as needles, which were filtered and washed twice with cold water, yield 22.7 g. IR: 3200 (N–H, m), 1218 (SO_3^-, s), 1180 (SO_3^-, s), 1058 (SO_3^-, s), and 816 cm^{-1} (1,4-, w—m).

Butylammonium (4-Methylphenyl)amidosulfate (9): An aqueous solution of ammonium (4-methylphenyl)amidosulfate was passed through a column of Dowex 50W×4 (butylammonium form) and the eluate was evaporated to a small volume, giving colorless *crystals*. These were filtered, washed with cold water, and dried. IR: 1512 (m), 1185 (SO_3^-, s), 1041 (SO_3^-, s), 895 (m), 820 (1, 4-, m), and 696 cm^{-1} (br, m). Found: N, 10.67; S, 12.23%. Calcd for $C_{11}H_{20}O_3N_2S$: N, 10.76; S, 12.31%.

4-Methylanilinium (4-Methylphenyl)amidosulfate (11): An aqueous solution of bis(4-methylanilinium) sulfate was added slowly to a stirred solution of barium (4-methylphenyl)amidosulfate (4.35 g) in water (50 ml) until no more precipitate was formed. After stirring for a short period, the precipitate was filtered and the filtrate was evaporated to dryness. The *product* was washed repeatedly with ether and dried in a desiccator over silica gel; glistening flakes. IR: 2915 (NH_3^+, br, m), 1517 (m), 1205 (SO_3^-, s), 1050 (SO_3^-, s), 897 (w), and 815 cm^{-1} (1,4-, m). Found: N, 9.49; S, 10.77%. Calcd for $C_{14}H_{18}N_2O_3S$: N, 9.52; S, 10.89%. Mp: 168—169.5 °C (depended on the rate of heating).

Tetraphenylphosphonium Chloride (16): This salt was prepared according to the procedure of Horner *et al.*[33] with a slight modification. IR: 1620 (w), 1583 (w), 1480 (w,) 1434 ($C_6H_5P^+$, m), 1311 (w), 1107 ($C_6H_5P^+$, s), 998 (m), 763

(m), 722 (s), and 688 cm^{-1} (m). Found: Cl, 9.42; P, 8.18%. Calcd for $C_{24}H_{20}ClP$: Cl, 9.46; P, 8.26%.

Preparation of Authentic Compounds. Sodium (4-Methylphenyl)amidosulfate: The sodium salt was obtained from the foregoing ammonium salt by passing through a cation-exchanger (Na^+ form) column. Recrystallization from methanol gave the pure *salt*. IR: 3260 (N–H, m), 1512 (m), 1198 (SO_3^-, s), 1061 (SO_3^-, s), 910 (m), and 810 cm^{-1} (1,4-, m). Found: N, 6.78; S, 15.00%. Calcd for $C_7H_8O_3NNaS$: N, 6.70; S, 15.33%.

Tetraphenylphosphonium (4-Methylphenyl)amidosulfate: A hot solution of **16** (550 mg) in 20 ml of water was added to a stirred solution of sodium (4-methylphenyl)amidosulfate (300 mg). The mixture was boiled for a short time and cooled slowly. The phosphonium salt was collected by filtration. Repeated recrystallization from water furnished a pure *sample*. Found: N, 2.67; P, 5.75; S, 6.25%. Calcd for $C_{31}H_{28}O_3PS$: N, 2.67; P, 5.89; S, 6.10%. IR: 3225 (N–H, w), 1440 (C_6H_5-P^+, m), 1395 (w), 1224 (SO_3^-, s), 1205 (SO_3^-, s), 1103 (C_6H_5-P^+, s), 1033 (SO_3^-, s), 881 (m), 827 (2H, m), 761 (m), 722 (s), and 686 cm^{-1} (br, m).

4-Methylaniline-2,6-disulfonic Acid and Its Salts: 4-Methylaniline-2-sulfonic acid (commercial reagent) (5.00 g) and freshly distilled chlorosulfuric acid (2.4 g) were mixed and the mixture was heated at 120 °C for 2 h and then at 140 °C (for 2 h) until the evolution of hydrogen chloride had subsided. After cooling, cracked ice was added carefully to the reaction mass. The resulting solution was neutralized with slurries of barium hydroxide, heated to boiling, and filtered while hot; the precipitate was washed repeatedly with hot water. The combined filtrate and washings were evaporated to dryness. The solid was recrystallized twice from hot water, yielding the pure *barium salt*. This was then converted to the corresponding free acid by passing through a column of Amberlite IR-120B (H^+ form); the eluate was neutralized with aqueous sodium hydroxide. The neutralized solution was then concentrated to a small volume (*ca.* 12 ml). 3 M HCl (7.0 ml) and hot alcohol (10 ml) were added with stirring while hot. The mixture was left overnight at room temperature. *Monosodium 4-methylaniline-2,6-disulfonate* separated out as white glistening crystals. IR: 1500 (w), 1460 (w), 1235 (SO_3^-, s), 1180 (SO_3^-, s), 1122 (w), 1045 (SO_3^-, s), 882 (1H, w), and 805 cm^{-1} (m). Found: N, 4.25; S, 19.72%. Calcd for $C_7H_8O_6NNaS \cdot 2H_2O$: N, 4.31; S, 19.71%.

The *bis(hexylammonium) salt* was prepared by neutralization of the free acid with hexylamine. Recrystallization from ethyl acetate–isopropyl alcohol (5: 2 v/v) gave a pure *specimen*; mp: 185—186 °C. IR: 1470 (m), 1210—1175 (br, s), 1028 (s), 886 (w), 802 (m), and 752 cm^{-1} (w). Found: N, 8.90; S, 13.68%. Calcd for $C_{19}H_{39}O_6N_3S_2$: N, 8.95; S, 13.65%.

4-Methylaniline-2,5-disulfonic Acid and Its Salts: This acid was prepared by the reaction between 4-methylaniline-3-sulfonic acid and chlorosulfuric acid. The product was isolated as the *barium salt* and purified by recrystallization from water.

The barium salt was converted into the sodium and bis(hexylammonium) salts by the same procedure as above *Monosodium salt*; IR: 1513 (w), 1483 (m), 1382 (w), 1225—1193 (SO_3^-, br, s), 1130 (s), 1030 (SO_3^-, s), 780 (w), and 650 cm^{-1} (s). Found: N, 4.28; S, 19.07%. Calcd for $C_7H_8NNaS_2 \cdot 2H_2O$: N, 4.31; S, 19.17%. *Bis(hexylammonium) salt*; mp: 195—196 °C. IR: 1480 (m), 1399 (m), 1202 (s), 1176 (s), 1118 (w), 1014 cm^{-1} (s). Found: N, 8.86; S, 13.34%.

Dipotassium, Disodium, and Bis(tetraphenylphosphonium) Salts of 4-Methylaniline-N,2-disulfonic Acid: Sulfur trioxide (2.14 g, 26.7 mmol) was dissolved in dry 1,2-dichloroethane (10 ml) and cooled in an ice–water bath. Dry 2-methylpyridine (3.0 ml) was added, drop by drop, with cooling and vigorous stirring. After stirring for 30 min, the solvent was removed *in vacuo* to give colorless crystals of 2-methylpyridine-sulfur trioxide adduct.

To the adduct was added in one portion an ice-cold solution of 4-methylaniline-2-sulfonic acid (4.60 g, 24.6 mmol) and potassium carbonate (3.70 g, 26.8 mmol) dissolved in water (40 ml). The mixture was allowed to warm to room temperature. Potassium carbonate (0.50 g, 3.6 mmol) was then added. After stirring at 35—40 °C for 30 min, the mixture was evaporated *in vacuo*, giving the solid. Recrystallization from 90% aqueous methanol gave the *potassium salt*. IR: 1485 (m), 1375 (w), 1281 (m), 1197 (SO_3^-, s), 1092 (s), 1047 (SO_3^-, s), 1027 (SO_3^-, s), 900 (w), 873 (w), 840 (w), and 706 cm^{-1} (m). Found: N, 3.50; S, 17.08%. Calcd for $C_7H_7O_6K_2NS_2 \cdot 2H_2O$: N, 3.69; S, 16.90%.

The dipotassium salt was converted to the disodium salt by cation-exchange. Recrystallization from aqueous ethanol yielded the pure *sodium salt*.[34] Found: N, 4.20; S, 19.47%. Calcd for $C_7H_7O_6NNa_2S_2 \cdot H_2O$: N, 4.25; S, 19.47%.

A solution of **16** (400 mg) in water (20 ml) was added to a stirred solution of the foregoing potassium salt (200 mg) in water and the mixture was boiled for a few minutes. After cooling, the crystals were filtered, washed with water, and recrystallized from water to give the pure *phosphonium salt* (340 mg); mp 210—211 °C (dec) (immersed in a bath preheated at 204 °C). IR: 1485 (m), 1439 ($C_6H_5P^+$, s), 1210 (SO_3^-, s), 1106 ($C_6H_5P^+$, s), 1036 (SO_3^-, s), 1019 (m), 898 (w), 847 (w), 834 (w), 762 (m), 721 (s), and 688 cm^{-1} (m). Found: P, 6.76; S, 6.81%. Calcd for $C_{55}H_{47}O_6NP_2S_2$: P, 6.56; S, 6.79%.

Isolation and Identification of the Reaction Products. Tetraphenylphosphonium (4-Methylphenyl)amidosulfate: The product mixture from the reaction of **8** at 100 °C for 17 h was dissolved in water (10—20 ml).[35] To the filtered solution was added **16** (200 mg) and the mixture was boiled for a short time. The clear solution was allowed to cool slowly[36] and left overnight at room temperature. The crystals which separated were collected by filtration and washed three times with cold water. Repeated recrystallization from water gave the pure *phosphonium salt*. The IR spectrum was entirely in accord with that of an authentic sample. Found: N, 2.58; P, 5.78; S, 6.26%. Calcd for $C_{31}H_{28}O_3NPS$: N, 2.67; P, 5.89; S, 6.10%.

Bis(tetraphenylphosphonium) 4-Methylaniline-N,2-disulfonate: Disodium 4-methylaniline-*N*,2-disulfonate[37] was isolated by liquid chromatography from the reaction of **5** at 130 °C for 8.5 h. To the filtered solution (20 ml) of this salt (0.205 g) was added **16** (0.504 g) and the mixture was boiled for a short period and allowed to cool slowly. The crystallized phosphonium salt was purified by repeated recrystallization from water; mp 210—211 °C. The mixed mp with an authentic specimen was not depressed. The IR spectrum agreed entirely with that of authentic material.

4-Methylaniline-2-sulfonic Acid and Its Hexylammonoum Salt: The sodium salt was separated by liquid chromatography from the product mixtures. To a hot solution (*ca.* 5 ml) of this salt (0.350 g) was added 3 M HCl (2 ml). The mixture was boiled for 20 min and cooled. The *free acid* separated out as colorless needles (hemihydrate). IR: 1550 (NH_3^+, w), 1498 (m), 1270—1290 (s, br), 1262 (w), 1092 (m), 1020 (s), 829 (m), and 698 cm^{-1} (m). Found: N, 7.12; S, 16.33%. Calcd for $C_7H_9O_3NS \cdot 1/2H_2O$: N, 7.14; S, 16.34%.

The free acid was neutralized with a methanolic solution of hexylamine. The solution was evaporated to dryness and the solid was recrystallized from EtOH–AcOEt (1: 1 v/v) to

give the pure *hexylammonium salt*: mp 208—209 °C, mixed mp 208—208.5 °C. The IR spectrum agreed entirely with that of an authentic sample.

Bis(hexylammonium) 4-Methylaniline-2,6-disulfonate: The crude disodium salt (0.30 g) was dissolved in water and the solution was passed through a column of Dowex 50WX4 (H^+ form). The eluate was neutralized with a methanolic solution of hexylamine. After evaporation, the solid was recrystallized from *i*-PrOH–AcOEt (1: 5 v/v) to give the *bis-(hexylammonium) salt* as fine needles; mp 185—186 °C, mixed mp with an authentic sample: 185.5—186 °C. The IR spectrum was in agreement with that of an authentic specimen.

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12) According to IUPAC rules this compound may be called (4-methyl-2-sulfophenyl)amidosulfate or *N*-(4-methyl-2-sulfophenyl)sulfamate.

13) The term "transsulfonation" in this paper refers to the transfer of a sulfonate group from one amino nitrogen to another amino nitrogen and the term "rearrangement" refers to the transfer of a sulfonate group from the aromatic amino-nitrogen to the aromatic ring.

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27) It is expected that the electron-donating effect of the sulfamino group is much smaller than that of the amino group.

28) The formation of **13** can be accounted for in terms of the deficiency of **6** in the reaction mixture, *i.e.* $\mathbf{6}/SO_3 < 1$) caused by partial deposition of **6** on the cool wall of the reaction vessel.

29) The position of this equilibrium is, of course, dependent on the steric factors. 2,6-Dimethylanilinium salt of butylamidosulfuric acid, for example, is unstable and dissociates into the acid and 2,6-dimethylaniline even at room temperature. Accordingly, this salt undergoes trans-sulfonation and rearrangement to 2,6-dimethylaniline-4-sulfonic acid far more readily than **5**. See a later paper.

30) We succeeded, however, in isolating (2,4,6-trimethylphenyl)imidobis(sulfate) from the thermal reaction of 2,4,6-trimethylanilinium butylamidosulfate; see a later paper.

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35) If the solution is acidic, it should be neutralized with 1 M ammonia.

36) If the phosphonium sulfonate tends to separate as an oil, sufficient water should be used for the crystallization and the solution should be seeded while hot.

37) This compound gave 4-methylaniline-2-sulfonic acid on acid hydrolysis.